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IP

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/375,605 08/17/99 SHORT

J DIVER1140

HM22/0126
GRAY CARY WARE & FREIDENRICH LLP
4365 EXECUTIVE DRIVE
SUITE 1600
SAN DIEGO CA 92121-2189

EXAMINER

NASHED, N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED:

7
01/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/375,605

Applicant(s)

Short, J. M.

Examiner
Nashaat T. Nashed

Group Art Unit
1652



☒ Responsive to communication(s) filed on Aug 17, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 17-40 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 17-40 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The application has been amended as requested in the communication filed March 28, 2k. Accordingly, claims 1-16 have been canceled, and claims 17-40 have been entered and under consideration.

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) and 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

The continuity data is confusing as there are two different statements after the title. The first is part of the original text of the application which claims a 119(e) benefit of provisional application 60/008,316 which was filed December 7, 1995 and indicating the application is a continuation in part of 08/651,568 filed August 3, 1998 [presumably May 22, 1996]. The second is introduced by amendment with the filing paper, see item number 5, indicating that the application is a continuation of 08/651,568. Please correct and clarify the continuity data and make it consistent with the declaration, i.e., "This application claim benefit from provisional application 60/008,316, filed December, 7, 1995, and is a continuation in part of 08/651,568, filed May 22, 1996, now U. S. Patent 5,939,250."

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the word "shuffling", presumed to mean "gene shuffling", in claim 21, 23, and 40 is not found in the original specification or the claims in the parent case, and therefore, it should be deleted.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The information disclosure statement filed 8/17/99 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office. It has been placed in the application file, but the information referred to therein has not been considered. There are three pages of PTO-1449 two of which are copies of the IDS filed in the parent case. In addition, four pages of form PTO-892 from the parent file. If applicant wishes that all references appeared on all 7 pages be considered, a proper IDS for PTO-1449 must be filed.

Claims 25 and 31 are objected to because it has identical scope to claims 23 and 24, respectively. Nucleic acid fragment shuffling and assembly PCR appear to be identical

methods. Also, according to the specification oligonucleotide-directed mutagenesis is defined as site specific mutagenesis, see page 13, paragraph 3. Claims 25 and 31 must be deleted or rewritten to have a different scope from those of claim 23, and 24, respectively.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-40 are rejected under the judicially created doctrine of double patenting over claims 1-12 of U. S. Patent No. 5,939,250 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The claims in the instant application are drawn to a method of identifying a protein having specific activity wherein said method comprising the step of screening a library(ies) comprising plurality of DNA isolated from heterogeneous population of source, isolating a clone with specified activity, subjecting the clone to random mutagenesis, and comparing the activity of the mutagen clone to that of the ordinarily isolated.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 17-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 5,958,672 (672') in view of the prior art as exemplified by Arnold *et al.* (U. S. Patent 5,316,935).

Arnold *et al.* teach random mutagenesis to obtain modified subtilisin enzymes by the production of mutant genes, their expression in transformed host cells and screening to identify enzymes with desired activities (see column 7, lines 40-59).

Since one of the ordinary skill in the art would have had the motivation to identify new and improved enzymatic activity at the time of invention, it would have been obvious to the ordinary skilled artisan practicing claims 1-15 in 672' to obtain new bioactivities to further random mutagenizing the gene encoding the desired activity and screen for desired characteristic such as improved thermal stability, enhances activity, or improved substrate specificity.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-40 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrases "heterologous population of DNA from more than one source" and "from either a single or a multiple source" in claim 17 render the claim indefinite and confusing because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The claim is drawn to a method of obtaining a specified protein or bioactivity of interest encoded by DNA contained in a heterogeneous population of DNA, see the preamble of the method. The first step in the method is screening a library contains a plurality of clones from a single source which is not heterologous DNA by definition. For examination purposes, the claim is interpreted a method of random mutagenesis of any gene of interest and the phrase "heterologous population" is taken to mean either a DNA from biological source or a DNA population obtained by random mutagenesis of any gene using any method.
- (b) The word "shuffling" in claims 21, 23 and 40 renders the claim indefinite and confusing because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The word is not defined in the specification and one of ordinary skill in the art would not know to what does

- it refer. The deletion of the word would overcome this rejection. For examination purposes the word is taken to mean "gene shuffling", a phrase which is not found in the specification or the original claims of the parent file.
- (c) the phrase "sexual PCR mutagenesis" in claims 21, 26, and 40 renders the claim indefinite and confusing because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. It is noted that the term is defined on page 13, paragraph 5, but the definition is confusing and one of ordinary skilled in the art would not know its meaning. The phrase is defined as being an *in vitro* method of mutagenesis whereas the word "sexual" refers to a biological process, i.e., *in vivo* method.
 - (d) The phrases "screening the heterogeneous population of DNA for further specified protein activity" in claim 32, and "heterogeneous population of DNA obtained from" in claims 34 and 35 render the claim indefinite and confusing because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. For examination purposes, it is assumed that: (a) the phrase "screening the heterogeneous population of DNA for further specified protein activity" is interpreted to mean "screening a DNA library comprising the heterogeneous population of DNA for further specified protein activity"; and (b) the methods of claims 34 and 35 are drawn to a method of obtaining desired mutant by random mutagenesis.
 - (e) claims 18-20, 22-25, 27-33, and 35-39 are included in this rejection because they are dependent on rejected claims and do not correct the deficiencies of the claim from which they depend.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-19, 21, 22, 24, 27, 28, 31-36, and 38-40 are rejected under 35 U.S.C. § 102(b) as being anticipated by Arnold *et al.* (U. S. Patent 5,316,935).

Arnold *et al.* a method of obtaining mutants of subtilisin with desired characteristics which includes random mutagenesis of the gene encoding the enzyme by various method including PCR and site directed mutagenesis, incorporate the mutated now heterologous population of genes into expression vectors, transform suitable cell, and screen for a colony expressing subtilisin mutant with desired characteristics, see from line 19, column 7 through column 8, line 61, and example I-VIII.

Claims 17-19, 21-25, 28, 31-36, and 38-40 are rejected under 35 U.S.C. § 102(b) as being anticipated by Stemmer *et al.* (U. S. Patent 5,605,793).

Stemmer *et al.* teach a method of identifying proteins having desired activity using nucleic acid shuffling mutation method, constructing a library and screening the library for desired activity, see Figure 1, and column 4, lines 49-60, from line 60, column 8 through line 24, column 9. Also, they teach the use of PCR primer, DNA fragments (cosset mutagenesis), DNA reassembly, and PCR error prone method to construct a library of mutants, see Figure 1 and examples 1-7.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 20, 21, 23, 25, 26, 29, 30, 37, and 40 are rejected under 35 U.S.C. § 103 as being unpatentable over Stemmer *et al.* in view of the state of the art as exemplified by the cited art, Delagrave *et al.* (Biotechnol. 1993, 11, 1548-1552), Arkin *et al.* (Proc. Natl. Acad. Sci. U. S. A. 1992, 89, 7811-7815), and Stemmer B (Stemmer *et al.* Proc. Natl. Acad. Sci. U. S. A. 1994, 91, 10747-10751).

The teaching of Stemmer *et al.* are summarized above.

Delagrave *et al.* teach the ensemble mutagenesis method, see the abstract.

Arkin *et al.* teach an algorithm for protein engineering named recursive ensemble mutagenesis, see abstract.

Stemmer B teach the nucleic acid shuffling/assembly PCR method.


Stemmer *et al.* provide one of ordinary skill in the art with a motivation to develop a method of identifying a protein with modified activity by generate a heterologous population of DNA from a gene encoding by mutagenesis, see column 4, lines 51-60. Thus, the ordinary skill in the art would have obtained a gene encoding a protein of interest, subjected the gene to one of several random mutation methods taught by any of Delagrave *et al.* Arkin *et al.*, Stemmer *et al.* and Stemmer B, construct an expression library comprising the heterologous DNA population, and screen for the desired improved activity as taught by Stemmer *et al.* (claims 21, 23, 25, 26, 29, 30, and 40). Once a clone is identified having the DNA encoding the desired activity, the DNA can isolated by hybridization methods using a complementary sequence attached to as solid support (claims 20 and 37). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday-Thursday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Nashaat T. Nashed, Ph. D.
Primary Examiner